

Deconstructing Tumor Heterogeneity: The Stromal Perspective

September 19 – 20, 2019
NCI Shady Grove, Room TE 406

Workshop Agenda

Goals and objectives

Significant advances have recently been made towards understanding the role of immune cell-tumor interplay in either suppressing or promoting tumor growth, progression, and recurrence. However, much remains to be explored and revealed concerning the important roles of additional stromal cell types, including fibroblasts, endothelial cells, adipocytes, and the influence of the extracellular matrix. The overarching goal of this workshop is to build upon advances in tumor-immune interactions and to highlight and integrate the critical functions of these non-immune stromal cell types within the context of their contribution to tumor heterogeneity and its resultant impact on tumor initiation, progression, and resistance to therapy. The workshop will:

- Explore the concept of tumor supportive vs tumor suppressive stroma and how cellular composition and function may be altered during disease progression
- Discuss mechanisms by which the microenvironment may promote indolence or drive aggressiveness of early lesions
- Highlight emerging themes of stromal plasticity and tumor-stromal crosstalk
- Understand how spatial geography impacts stromal attributes and function
- Deliberate on the prognostic-therapeutic implications and potential vulnerabilities within the heterogeneous tumor microenvironment
- Facilitate discussion and collaboration among researchers investigating diverse aspects of stromal biology
- Identify current challenges and knowledge gaps in the field

Co-Chairs: Dr. Sheila Stewart, Washington University in St. Louis School of Medicine
Dr. Simon Hayward, NorthShore University Health System/University of Chicago

Day 1 September 19, 2019

07:30 Registration

08:00-08:30 **Welcome and workshop overview**

Program Objectives: **Jeff Hildesheim**, DCB, NCI

Opening Remarks: **Dinah Singer**, Deputy Director, NCI

Simon Hayward, NorthShore U Health System
 University of Chicago

Session 1: Stromal-centric arbiters of tumor progression and suppression

Chair: Simon Hayward

08:30-08:55 **Functional Heterogeneity of Fibroblasts and Type I Collagen in Pancreatic Cancer**
 Raghu Kalluri, University of Texas, MD Anderson

08:55-09:20 **Fibroblast Heterogeneity and Interactions with Periprostatic Fat as Mediators of Prostate Cancer Progression**
 Simon Hayward, NorthShore University HealthSystem
 University of Chicago

09:20-09:45 **Age Against the Machine: How Aging Disrupts the Homeostasis of the Stromal Microenvironment to Promote Tumor Progression**
 Ashani Weeraratna, Johns Hopkins Bloomberg School
 of Public Health

09:45-10:10 **Mechanisms that Drive the Stromagenic Switch and CAF Heterogeneity**
 Ellen Puré, University of Pennsylvania

10:10-10:35 **Fibroblast Diversity in Pancreatic Cancer**
 David Tuveson, Cold Spring Harbor Laboratory

10:35-10:55 Discussion

10:55-11:15 Break

Session 2: Biology of early lesions: indolence vs aggressiveness

Chair: Sheila Stewart

11:15-11:40 **Stromal Suppression of Tumor Growth in Tumors of Endodermal Derivation**
 Phil Beachy, Stanford Institute for Stem Cell Biology &
 Regenerative Medicine

- 11:40-12:05 **Tissue Tumor Hotspot: Terroir for Tumorigenesis**
Wu-Min Deng, Tulane University School of Medicine
- 12:05-12:30 **Computational Modeling of Single-Cell Data Identifies Cancer-Associated Fibroblasts Interactions with Tumor Cells to Drive the Progression of Colonic Adenomas**
Ken Lau, Vanderbilt University Medical Center
- 12:30-12:55 **Mechanisms and Consequences of Pancreatic Cancer Stromal Evolution**
Mara Sherman, Oregon Health and Science University
- 12:55-13:15 Discussion
- 13:15-14:15 Lunch (on your own)

Session 3: Stromal plasticity and communication

Chair: Simon Hayward

- 14:15-14:40 **New Players of the Stroma-Epithelium Crosstalk in Mesenchymal Colorectal Cancer**
Jorge Moscat, Sanford Burnham Institute
- 14:40-15:05 **Deconstructing Adipogenic Niches with scRNA Sequencing: Implications for Stromal-Tumor Immune Cell Interactions**
James Granneman, Wayne State University
- 15:05-15:30 **Acquisition of Tumor Heterogeneity Through Neoplastic Cell-Macrophage Fusion**
Melissa Wong, Oregon Health & Science University
- 15:30-15:40 Break
- 15:40-16:05 **Applying Micro Scale Models to Explore Cancer Heterogeneity at Multiple Levels**
David Beebe, University of Wisconsin, Madison
- 16:05-16:30 **Modeling Tumor/Microenvironment Interactions Using the Zebrafish**
Richard White, Memorial Sloan Kettering
- 16:30-16:55 **Stromal Contributions to Ovarian Cancer Metastasis**
Ernst Lengyel, The University of Chicago
- 16:55-17:15 Discussion
- Adjourn
- 18:00-20:00 Dinner (on your own, organized by Chairs)**

Day 2 September 20, 2019

Session 4: Geography and architecture matters

Chair: Sheila Stewart

- 09:00-09:25 **Endothelial Heterogeneity and Vascular Engineering Models**
Ying Zheng, University of Washington
- 09:25-09:50 **Data Driven Annotation of Tumors and its Microenvironment
by Transcriptome Analysis *In Situ***
Joakim Lundeberg, KTH Royal Institute of Technology, Sweden
- 09:50-10:15 **Cancer-Associated Fibroblast Subtypes in Control of
Malignant Phenotypes**
Kristian Pietras, Lund University, Sweden
- 10:15-10:30 Break
- 10:30-10:55 **The Microenvironment and Resistance to Targeted Therapies
in Lung Cancer**
Katerina Politi, Yale School of Medicine
- 10:55-11:20 **Cancer Associated Fibroblast Heterogeneity in Breast Cancer**
Ruth Scherz-Shouval, Weizmann Institute of Science
- 11:20-11:50 Discussion
- 11:50-13:00 Lunch (on your own)

Session 5: Prognostic and therapeutic implications of microenvironmental heterogeneity

Chair: Simon Hayward

- 13:00-13:25 **Senescence Drives Chemotherapy-Induced Bone Loss**
Sheila Stewart, Washington University School of Medicine
- 13:25-13:50 **Programming of Cancer Associated Fibroblasts Potentiate a
Paracrine Signaling Loop that Confers Taxane Resistance**
Neil Bhowmick, Cedars-Sinai
- 13:50-14:15 **Functional Heterogeneity of Pancreatic Cancer-Associated
Fibroblast and Allied ECMs: Outcome Indicators**
Edna Cukierman, Fox Chase Cancer Center
- 14:15-14:40 **Therapeutic Implications of Tumor Microenvironment
Constituents as Drivers of Cancer Therapy Resistance**
Peter Nelson, Fred Hutchinson Cancer Center
- 14:40-15:05 Discussion

Closing: 15:05-15:30 Wrap-up (state of the science, prioritization of the challenges ahead, and emerging directions)
Sheila Stewart, Workshop Co-Chair, Washington University
School of Medicine